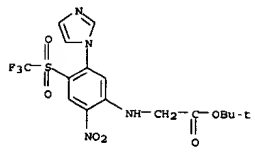
L5 ANSWER 16 OF 56 CAPLUS COPYRIGHT 2002 ACS (Continued)

AB The title compds. [I; X = N or CH; R = imidazolyl or di(lower alkyl)amino; R1 = (1) halo, nitro, cyano, carboxy, amino, mono- or di(lower alkyl)amino, lower alkanoyl, lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, or carbamoyl, (2) lower alkyl or lower alkoxy which may be substituted by halo, carboxy or aryl, or (3) phenyloxy which may be substituted by lower alkoxycarbonyl or carboxy; R2 = hydroxy, lower alkoxy, amino, or mono- or di(lower alkyl)amino; A = optionally substituted alkylene or O-B (B being lower alkylene); provided the case wherein R represents imidazolyl, R1 represents cyano, A represents ethylene and R2 represents hydroxy is excepted], which have high affinity for AMPA receptor of non-NMDA receptor and high soly. and suppress audiogenic convulsion, are prepd. A glutamate receptor antagonist, NMDA-glycine receptor and/or AMPA receptor antagonist, a kainate neurocytotoxicity inhibitor, a psychotropic, and a remedy for ischemia contains I. Thus, 2,4-difluoronitrobenzene was added to a mixt. of Et glycinate hydrochloride, Et3N, and THF and refluxed for 3 h to give 71.5% Et N-(2-nitro-5-fluorophenyl)glycinate, which was hydrogenated in the presence of 10% Pd-C in MeOH and stirred with Et chloroglyoxylate and Et3N in CHCl3 at room temp. for 1 h to give 80% Et 2-(7-fluoro-2,3-dioxo-1,2,3,4-tetrahydroquinoxalin-1-yl)acetate. The latter compd. was nitrated by fuming HNO3 in concd. H2SO4 to give 96% Et 2-(7-fluoro-6-nitro-2,3-dioxo-1,2,3,4-tetrahydroquinoxalin-1-yl)acetate, which was heated with **imidazole** in DMF at 120.degree. for 6 h followed by sapon. with 1 N aq. NaOH and acidification with 1 N aq. HCl to pH .apprx.3.5 to give the title compd. (II; R1 = NO2). The latter compd. and II (R1 = PhCH2O) in vitro inhibited the binding of [3H]-AMPA to rat cerebral membrane sample with Ki value of 0.093 and 0.07 .mu.M, resp. A vial formulation contg. II (R1 = NO2) was described.

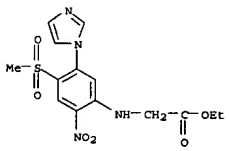
IT **179010-91-4P 179011-18-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of tetrahydroquinoxalinedione deriva. as NMDA-glycine receptor and/or AMPA receptor antagonists, kainate neurocytotoxicity inhibitors, psychotropics, and ischemia remedy)

RN 179010-91-4 CAPLUS
CN Glycine, N-[5-(1H-imidazol-1-yl)-2-nitro-4-[(trifluoromethyl)sulfonyl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

L5 ANSWER 16 OF 56 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 179011-18-8 CAPLUS
CN Glycine, N-[5-(1H-imidazol-1-yl)-4-(methylsulfonyl)-2-nitrophenyl]-, ethyl ester (9CI) (CA INDEX NAME)



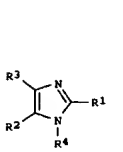
L5 ANSWER 17 OF 56 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:367336 CAPLUS
DOCUMENT NUMBER: 125:33647
TITLE: 4,5-Substituted imidazolyl compounds for the treatment of inflammation
INVENTOR(S): Weier, Richard M.; Collins, Paul W.; Stealey, Michael A.; Barta, Thomas E.; Huff, Renee M.
PATENT ASSIGNEE(S): G.D. Searle and Co., USA
SOURCE: PCT Int. Appl., 226 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

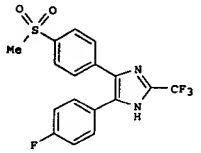
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9603387	A1	19960208	WO 1995-US9505	19950727
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5620999	A	19970415	US 1994-281903	19940728
CA 2195846	AA	19960208	CA 1995-2195846	19950727
AU 9532716	A1	19960222	AU 1995-32716	19950727
EP 772601	A1	19970514	EP 1995-929327	19950727
EP 772601	B1	20020918		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
EP 1211244	A2	20020605	EP 2002-2833	19950727
EP 1211244	A3	20020612		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
US 6426360	B1	20020730	US 2000-571033	20000515

PRIORITY APPLN. INFO.: US 1994-281903 A 19940728
EP 1995-929327 A3 19950727
WO 1995-US9505 W 19950727
US 1997-765865 B1 19970110
US 1998-218208 B1 19981222

OTHER SOURCE(S): MARPAT 125:33647
GI



I



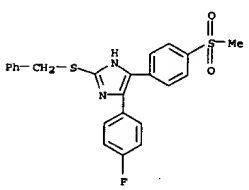
II

L5 ANSWER 17 OF 56 CAPLUS COPYRIGHT 2002 ACS (Continued)

AB A class of **imidazoles** is described, useful for treatment of inflammation and related disorders (arthritis, pain, and fever). Compds. of particular interest are I [R1 = (un)substituted alkyl, SH, substituted carbonyl or sulfonyl, aralkenyl, 2-thienyl, 2-furyl, 3-furyl, 2-pyridyl, 4-pyridyl and 2-benzofuryl; R2, R3 = (un)substituted heteroaryl, cycloalkyl, or aryl; R4 = H, alkyl, or acyl] and pharmaceutically acceptable salts. Examples include 95 compds. and their prepn., in vivo assays of 3 compds., and screening data of most compds. for selective inhibition of human recombinant cyclooxygenase 2 in vitro. For instance, condensation of 4-FC6H4CH2CO2H with 4-(MeS)C6H4CHO (50%) gave a mixt. of cis- and trans-stilbenes 4-(MeS)C6H4CH:C(CO2H)C6H4F-4. Reaction of this with (PhO)2P(O)N3, followed by heating in PhMe and acid hydrolysis, gave 65% 4-(MeS)C6H4CH2COC6H4F-4. The latter underwent S-oxidn. to the sulfone (80%), alpha.-oxidn. with H2SeO3 to an .alpha.,.beta.-diketone (60%), and cyclocondensation with NH4OAc and CF3CH(OH)OEt (34%), to give title compd. II. In the carrageenan-induced rat paw edema and analgesia tests, II at 30 mg/kg orally gave 22% inhibition of edema, and 25% inhibition of hyperalgesic foot withdrawal.

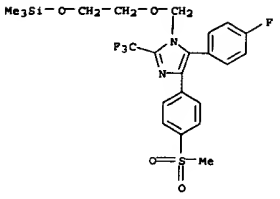
IT **177754-49-3P 177755-75-8P 177755-76-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; prepn. of **imidazole** deriva. as antiinflammatories)

RN 177754-49-3 CAPLUS
CN 1H-Imidazole, 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-2-[(phenylmethyl)thio]- (9CI) (CA INDEX NAME)

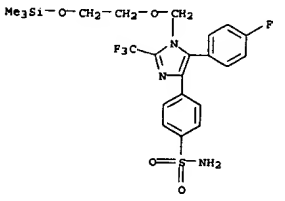


RN 177755-75-8 CAPLUS
CN 1H-Imidazole, 5-(4-fluorophenyl)-4-[4-(methylsulfonyl)phenyl]-2-(trifluoromethyl)-1-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]- (9CI) (CA INDEX NAME)

L5 ANSWER 17 OF 56 CAPLUS COPYRIGHT 2002 ACS (Continued)

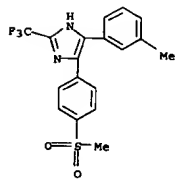


RN 177755-76-9 CAPLUS
CN Benzenesulfonamide, 4-[5-(4-fluorophenyl)-2-(trifluoromethyl)-1-[[2-[(trimethylsilyl)oxy]ethoxy]methyl]-1H-imidazol-4-yl]- (9CI) (CA INDEX NAME)



IT 177754-42-6P 177754-94-8P 177754-99-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of imidazole derivs. as antiinflammatories)
RN 177754-42-6 CAPLUS
CN 1H-Imidazole, 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

L5 ANSWER 17 OF 56 CAPLUS COPYRIGHT 2002 ACS (Continued)



IT 177754-43-7P 177754-44-8P 177754-45-9P
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177754-52-8P 177754-53-9P 177754-54-0P
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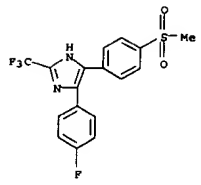
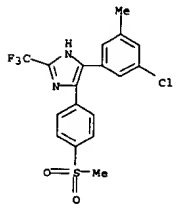
177755-26-9P 177755-27-0P 177755-28-1P
177755-29-2P 177755-30-5P 177755-31-6P
177755-32-7P 177755-33-8P 177755-34-9P
177755-35-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of imidazole derivs. as antiinflammatories)
RN 177754-43-7 CAPLUS
CN 1H-Imidazole, 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-2-(phenoxymethyl)- (9CI) (CA INDEX NAME)

L5 ANSWER 17 OF 56 CAPLUS COPYRIGHT 2002 ACS (Continued)

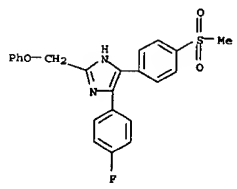


RN 177754-94-8 CAPLUS
CN 1H-Imidazole, 4-(3-chloro-5-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



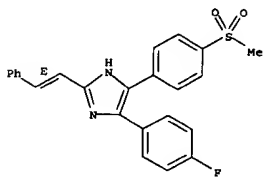
RN 177754-99-3 CAPLUS
CN 1H-Imidazole, 4-(3-methylphenyl)-5-[4-(methylsulfonyl)phenyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

L5 ANSWER 17 OF 56 CAPLUS COPYRIGHT 2002 ACS (Continued)

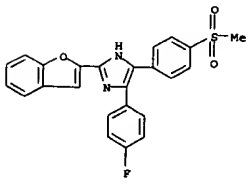


RN 177754-44-8 CAPLUS
CN 1H-Imidazole, 4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]-2-(2-phenylethenyl)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 177754-45-9 CAPLUS
CN 1H-Imidazole, 2-(2-benzofuranyl)-4-(4-fluorophenyl)-5-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



RN 177754-46-0 CAPLUS
CN 1H-Imidazole, 4-(4-fluorophenyl)-2-(1-methylethyl)-5-[4-